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Autosomal Dominant Familial Radial Luxation, Carpal Fusion and Scapular Dysplasia With Variable Heart Defects

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A family is described with skeletal abnormalities involving the shoulder, elbow, and hand, in combination with variable cardiac defects including conduction defects and anatomical anomalies. The disorder followed an autosomal dominant pattern of inheritance with apparently full penetrance for the skeletal abnormalities and reduced penetrance for the cardiac defects.

KEY WORDS: carpal fusion, radial luxation, shoulder dysplasia, anatomical cardiac defects, arrhythmia, autosomal dominant, metacarpo-phalangeal profile (MCPP)

INTRODUCTION

There are several entities known to combine skeletal and cardiac malformations, e.g., Holt-Oram syndrome [Hurst et al., 1991; Boehme and Shotar, 1989], heart-hand syndrome type II [Silengo et al., 1990; Temtamy and McKusick, 1978], heart-hand syndrome type III [Ruiz de la Fuente and Prieto, 1980], the long thumb-brachydactyly syndrome [Hollister and Hollister, 1981], humerospinal dysostosis with congenital heart disease [Kozlowski et al., 1974], Ebstein's anomaly-skeletal anomalies [Balaji et al., 1991], brachydactyly type E with atrial septal defect [Czeizel and Goblyos, 1989], camptodactyly-arthritis-pericarditis [Athreya and Schumacher, 1978; Laxer et al., 1986], the upper limb-cardiovascular syndrome [Di Bella et al., 1984] and the case reports by Liebenberg [1973], Jones et al. [1973] and Bonneau et al. [1983].

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Here we report on a family in which a comparable but probably still different combination of upper limb anomalies and variable cardiac defects was segregating as an autosomal dominant trait.

CLINICAL REPORTS

The proposita (Fig. 1; III-14) was referred to our Institute because she had congenital anomalies of the upper limbs, and several relatives had cardiac disorders. She had 3 children and 2 miscarriages with 2 different partners; one son (Fig. 1; IV-10) had similar skeletal abnormalities which did not impair normal daily activities. Physical examination did not show other significant defects in the proposita or her son. Supination of forearms was moderately limited (more so in the boy), as was the function of the thumbs. Although the proposita had complaints of occasional dizziness and an irregular heartbeat, a full cardiac examination showed only a minimal end-systolic prolapse of the mitral valve. Plasma cholesterol and triglyceride levels were normal.

Roentgenographs of the upper limbs of the proposita showed a fusion between lunate and triquetrum and between scaphoid and trapezoid (Fig. 2). The ulna was elongated, and the styloid process was absent. The radial head was slightly deformed and luxated. There was a mild S-shaped scoliosis of the vertebral column, without clear vertebral anomalies.

In her son a slightly delayed bone age was present (1 year behind at a calendral age of almost 6 years), but no signs of any carpal fusion. The radial heads were luxated bilaterally (Fig. 3). The spine showed a moderate thoracolumbar scoliosis. Cardiac examination demonstrated a minimally prolonged QRS time, but no other rhythm disturbances or sonographically detectable abnormalities.

An older brother of the proposita (Fig. 1; III-12) was born as one of twins; his twin brother had died on the first day of life without known cause. There was no reliable information on his skeletal status. The brother had the same skeletal abnormalities as his sister. Furthermore, he had an ASD and rhythm disturbances, including an incomplete right bundle branch block and paroxysmal atrial fibrillation. His son (Fig. 1; IV-7) had

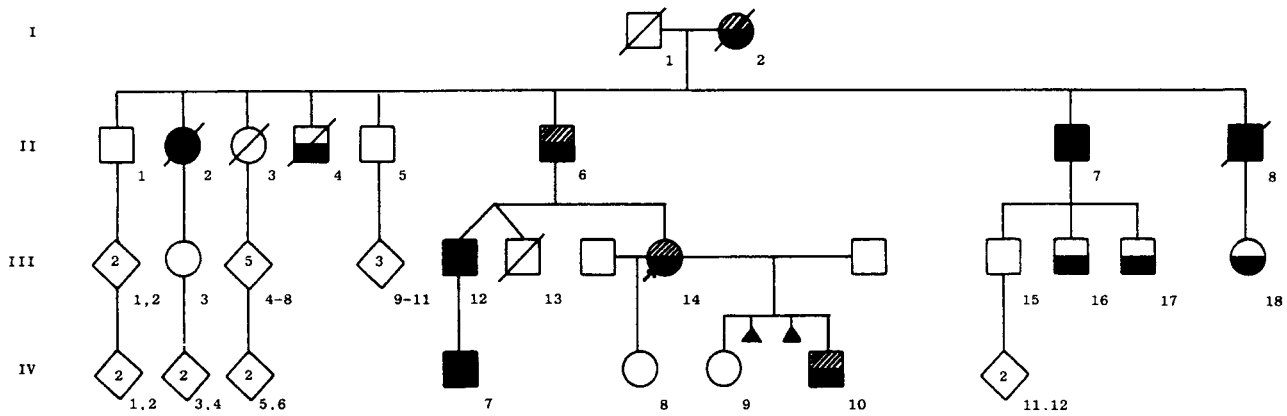

Fig. 1. Pedigree of the family: ▬, skeletal anomaly; ■, skeletal and heart anomaly; ▨, mild/dubious heart anomaly.

the same skeletal findings, and was born with a VSD. The proposita's father (Fig. 1; II-6) had carpal fusions, radial luxation, an S-shaped thoracolumbar scoliosis, and a short and deformed scapula. He had had 3 myocardial infarctions, the first one at 45 years, and rhythm disturbances (atrial fibrillation and incomplete right bundle branch block), but possibly these were the consequence of earlier infarctions. One of his sisters (Fig. 1; II-2) and one of his brothers (Fig. 1; II-8) had both died of a "cardiac abnormality" at the age of 30 years and 35 years, respectively. Both were said to have had limited movements in their elbows. Unfortunately, more detailed information on cardiac or skeletal status was unavailable. The daughter of II-8 (Fig. 1; III-18) had the skeletal anomalies, but no cardiac complaints. Another brother (Fig. 1; II-7) had skeletal and cardiac involvement including a paroxysmal atrial flutter for which he received a pacemaker in his twenties. He had two sons (Fig. 1; III-16, III-17) with skeletal symptoms but no apparent heart defects. A third brother of the proposita's father (Fig. 1; II-4) had the same skeletal anomalies as the proposita, and in addition a short and deformed scapula. He had died at the age of 62 years, probably because of an infarction. The grandmother (Fig. 1; I-2) had died at over 80 years, and was reported to have had the same skeletal anomalies. She was known to have had cardiac problems, but exact data were again missing (Table I).

Fig. 2. X-rays of the hands of the proposita. Note the carpal synostoses, elongated ulna, and absent styloid process.

Metacarpo-phalangeal profile (MCPP) analysis was possible in 4 of the affected relatives (III-14; III-12; II-4; II-7; see Fig. 4). The proposita had short metacarpals, fifth proximal phalanx, and distal phalanges; the third proximal and medial phalanx were relatively long. The brother, III-12, had a comparable profile, although the third distal phalanx was relatively longer than in his sister. In II-7 all phalanges were longer than in III-14 and II-12, but the metacarpals remained short, and this was also true for II-4. The correlation coefficients for the Z-scores were .65, .43, .86, and .90 for III-14, III-12, II-4, and II-7, respectively.

DISCUSSION

Carpal synostosis in combination with limited movement of the elbow, dislocation of the elbow, or shoulder, radial hypoplasia, and cardiac anomalies, has been described in a number of syndromes and case reports. The report by Kozlowski et al. [1974], in which anomalies of the urinary tract and vertebral anomalies were mentioned, the report by Hurst et al. [1988], in which the proband had microcephaly and an abnormal facial appearance, and the report by Tamari and Goodman [1974], which mentioned short stature, mental retardation, abnormal face and asymmetry of the limbs as

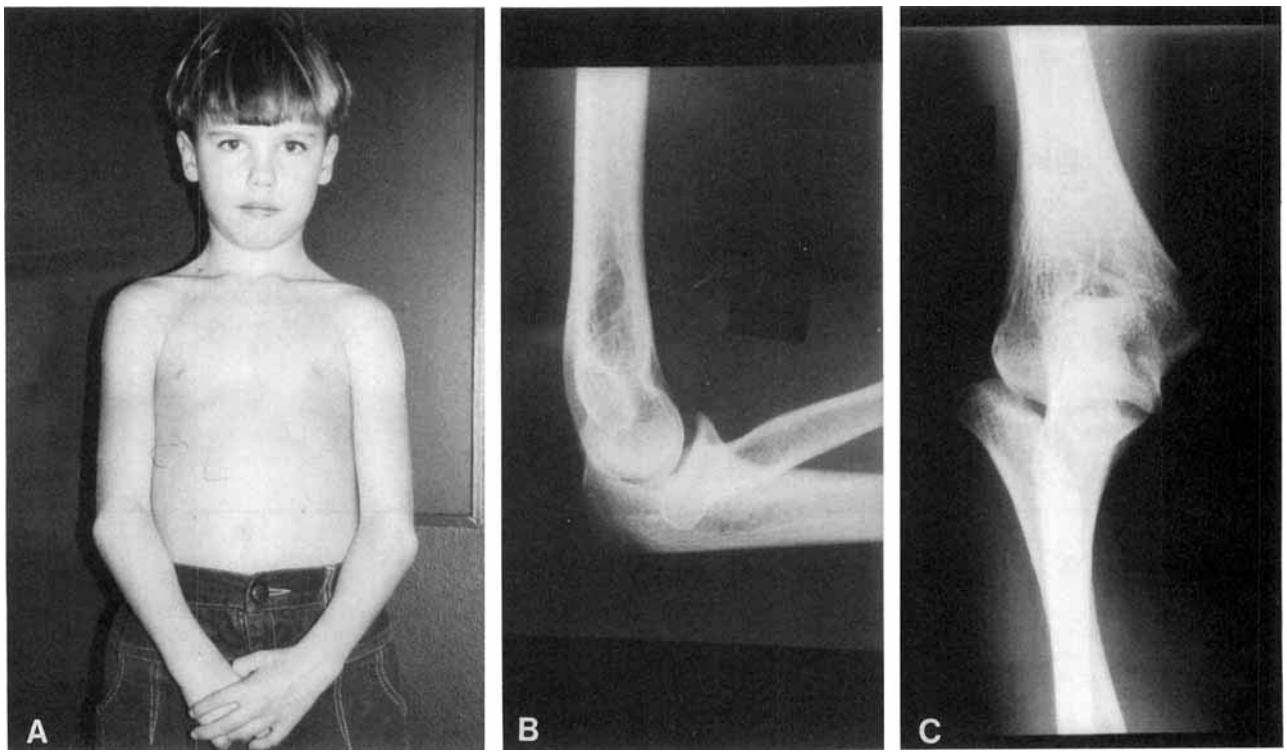

Fig. 3. **B,C:** X-rays of the upper limb of the son (IV-10; **A**) of the proposita. Note bilateral radial luxations.

other symptoms, are likely to represent different conditions because of the additional findings, not present in our family. Syndromes and case reports that resemble our family most are the Holt-Oram syndrome [Hurst et al., 1991; Boehme and Sotar, 1989], heart-hand syndrome type II (Tabatznik type) [Silengo et al., 1990; Temtamy and McKusick, 1978] and the case reports by Jones et al. [1973], and Liebenberg [1973]. These syndromes are compared to our family in Table II.

In the Holt-Oram syndrome, there is a variety of heart defects, including conduction defects. Carpal synostosis, restriction of supination/pronation, shoulder joint anomalies and scoliosis have all been found in Holt-Oram syndrome and in our patients. However, in Holt-Oram syndrome, the thumbs are often involved, as are the clavicles and pectoral muscles. In none of the affected members of our family did we find thumb, pectoral or clavicle anomalies. In the heart-hand syn-

TABLE I. Summary of the Skeletal and Cardiac Findings in the Present Family*

Family member	Heart rhythm disturbance[a]	Radial luxation	Carpal synostosis	Scoliosis	Other anomalies
I-2	(+)	(+)	?	?	
II-2	(+)	(+)	?	(−)	
II-4	+	+	+	+	c.s.[b]
II-6	+	+	+	+	c.s.[b]
II-7	+	+	+	+	
II-8	(+)	(+)	?	(−)	
III-12	+/ASD	(+)	?	(−)	
III-14	−	+	+	+	
III-16	?	(+)	?	(−)	
III-17	?	(+)	?	(−)	
III-18	?	(+)	?	(−)	
IV-7	VSD	(+)	?	(−)	
IV-10	−	+	−	+	

* +, positive; (+), anamnestically positive; −, negative; (−), anamnestically negative; ?, no data available.
[a] ASD, atrial septal defect; VSD, ventricular septal defect.
[b] Deformed and shortened collum scapuli.

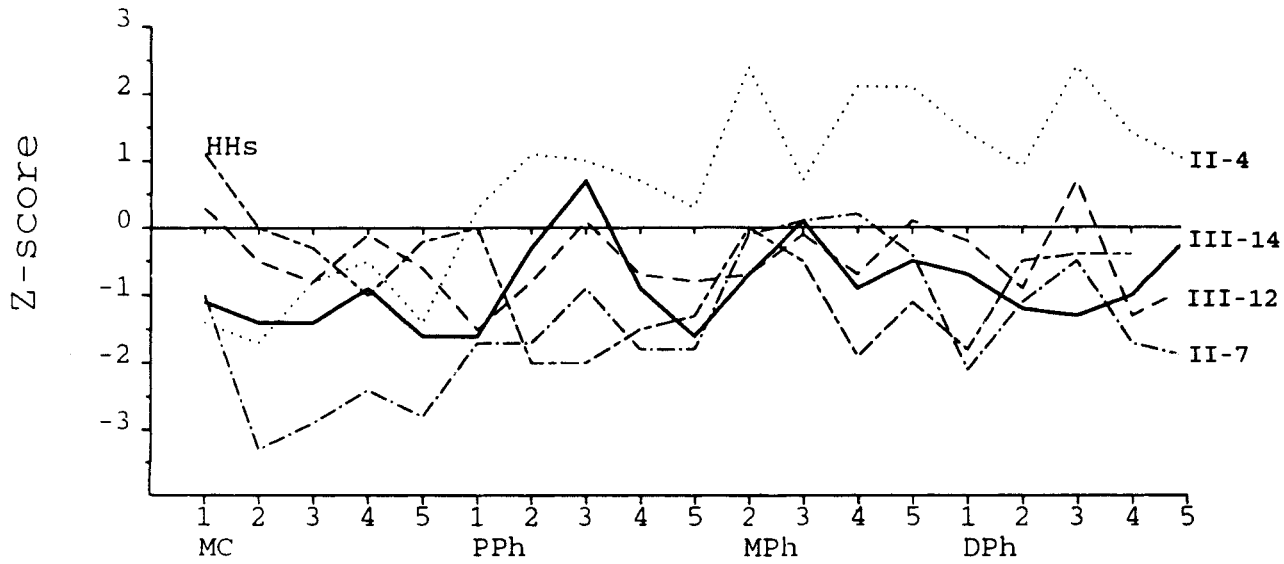

Fig. 4. Metacarpo-phalangeal profile (MCPP) analysis of the present family compared to an MCPP made from the X-ray of patient with heart-hand syndrome type II, published by Silengo et al. [1990]. MC, metacarpal; PPh, proximal phalanx; MPh, medial phalanx; DPh, distal phalanx; HHs, heart-hand syndrome.

drome, Tabatznik type, there are carpal synostosis, limited movement in the elbows and heart conduction defects, presenting as paroxysmal atrial tachycardia and fibrillation. The main point of difference is the brachydactyly, as shown by comparing the MCPP of Silengo et al.'s [1990] patient with heart-hand syndrome type II and the present family (Fig. 4; a comparison with the patients reported by Temtamy and McKusick was impossible due to insufficient quality of the published hand films). Other minor differences may be bowing of the radial and ulnar shafts, sloping shoulders with hypoplastic deltoid muscles and short arms, not found in our patients. Liebenberg [1973] described a family of individuals with carpal synostosis, mild limitation of movement of the elbows, and a restriction of supination-pronation. However, limited wrist move-

TABLE II. Symptoms Found in the Present Family Compared to Those Found in Similar Entities

	Present family	Liebenberg [1973][a]	Jones et al. [1973][b]	Holt-Oram synd.[c]	Heart-hand synd.[d]
Clinical symptoms					
Brachydactyly	−	+[e]	±	−	+
Thumb a/hypoplasia	−	−	−	+	+
(Hypo)thenar hypoplasia	−	+	−	+	−
Diminished elbow movements	+	+	+	+	+
Short upper limbs	−	−	−	−	+
Scoliosis	±	−	−	±	−
Hyperlordosis/kyphosis	−	−	+	+	−
Conduction defects	+	−	−	+	+
Structural heart defects	+	−	−	+	−
Short stature	−	−	+	−	−
Roentgenographic findings					
Carpal synostosis	+	+	+	±	±
Short metacarpals IV/V	−	−	−	−	+
Radial head luxation	+	+	−	−	−
Dysplastic distal ulna	+	−	−	+	+
Dysplasia collum scapulae	±	−	−	−	±
Other[a–d]	−	+	+	+	+

[a] Liebenberg [1973]: large carpals, hypoplastic nails.
[b] Jones et al. [1973]: narrowed intervertebral spaces, vertebral fusion, crowded ribs, flat feet.
[c] Holt-Oram: radial-ulnar synostosis, pectus excavatum/carinatum.
[d] Heart-hand syndrome type II: ulnar displacement, sloping shoulders, hypoplasia m. deltoideus, cryptorchidism, ear anomalies.
[e] +, present; ±, sometimes present; −, absent/not described.

ments, brachydactyly, and hypoplasia of the thenar and hypothenar were also present, and X-ray films showed involvement of the humerus and ulna. Jones et al. [1973] also described a syndrome with a restriction in pronation and supination, and fusion of two of the carpal bones, but also short trunk stature, and narrow intervertebral spaces.

The anomalies found in our patients consist of a constant (sub)luxation of the radial head with a limitation of pronation and supination, and carpal fusion in all members that could be evaluated roentgenographically. In some of the affected members this was accompanied by dysplasia of the collum scapulae and scoliosis. Not all the affected relatives had cardiac involvement, and those that were affected showed a large variation in symptomatology. The most frequently occurring manifestation was a conduction defect. None of the persons without skeletal symptoms had cardiac problems. It remains possible that conduction defects will turn out to be more frequent, as some of the younger affected relatives have not been fully investigated and clinical problems may become evident at a later age.

In conclusion, the present family may well have a hitherto undescribed cardiac-upper limb syndrome. The pattern of inheritance is compatible with the action of an autosomal dominant gene, with full penetrance for the skeletal anomalies and a decreased penetrance for the cardiac defects.

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